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TITLE: Improving Symptoms Control, QOL, and Quality of Care for  
Women with Breast Cancer: Developing a Research Program on  
Neurological Effects via Doctoral Education

PRINCIPAL INVESTIGATOR: Marie Bakitas  
Tim A. Ahles, Ph.D.

CONTRACTING ORGANIZATION: Dartmouth College  
Hanover, New Hampshire 03755-1404

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**6. AUTHOR(S)**Marie Bakitas  
Tim A. Ahles, Ph.D.**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**Dartmouth College  
Hanover, New Hampshire 03755-1404**E-Mail:** marie.whedon@hitchcock.org**8. PERFORMING ORGANIZATION  
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The purpose of this traineeship is to develop the academic, clinical, and research skills of an expert advanced practice nurse within the context of a mentor's (Tim A. Ahles, Ph.D.) funded program of research of the (central nervous system [CNS]) Cognitive Effects of Chemotherapy. The scope of the program is to support Ms. Bakitas' doctoral education with an ultimate career goal of becoming a Clinical Breast Cancer Research Scientist. In conjunction with the doctoral program, through a mentored research experience Ms. Bakitas is expanding an established research program on CNS effects of breast cancer treatment by developing a parallel focus on the peripheral nervous system effects of chemotherapy, (Chemotherapy-Induced Peripheral Neuropathy [CIPN]), on quality of life. The major achievements of the trainee at the midterm, are successful accomplishment of the planned training activities/tasks originally outlined for the first year, with an additional achievement of developing (as a co-investigator), a funded grant on chemotherapy induced peripheral neuropathy. The significance of these achievements is that the training is providing the initial foundation for developing a clinical nurse expert towards a program of breast cancer researcher.

**14. SUBJECT TERMS**

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- F. Literature Reviewed for Conceptual Model and Dissertation Proposal

## **Introduction**

This training grant proposed an interdisciplinary, mentored, clinical research experience on the understudied area of neurological effects of breast cancer treatment through a doctoral training program. The traineeship is based at two campuses: the Dartmouth Medical School/Norris Cotton Cancer Center, Lebanon, NH and Yale University, New Haven, CT. The trainee's research mentor, Tim Ahles, PhD, Director of Psycho-oncology Research, Norris Cotton Cancer Center supervises the trainee's clinical research skill development at Dartmouth and Doctoral Program Dean, Ruth McCorkle, PhD and Professor and dissertation chair, Tish Knobf, RN, PhD supervise the academic and research components at Yale University. The purpose of this traineeship is to develop, the academic, clinical, and research skills within the context of a doctoral nursing program and funded program of research of the (central nervous system) Cognitive Effects of Chemotherapy, to support Ms. Bakitas in the long term career goal of developing as a Clinical Breast Cancer Research Scientist. Through this traineeship Ms. Bakitas is expanding the Center for Psycho-oncology Program's focus on Central Nervous System/Cognitive Effects, by developing an independent, but parallel focus on the peripheral nervous system effects of chemotherapy (Chemotherapy-Induced Peripheral Neuropathy [CIPN]) on quality of life.

## **Body**

This section is organized according to the original Statement of Work (Appendix A) Achievements are reviewed and summarized for each of the original three tasks. Please note that original timeline was developed with an anticipated start date of Month 1= January 03. As funding was not actually available until April 03, there is occasional slight variation in the actual date of accomplishment; however all activities are on schedule within the 2 year grant period.

### **Task 1. Develop research skills and abilities, including measurement, data analysis, and conceptual model development in breast cancer research through mentorship and doctoral education. (Months 1-18)**

The trainee has successfully completed all of the proposed tasks according to the timeline. Research skill development activities have included research supervision by traineeship mentor Tim Ahles, PhD (at Dartmouth) and Yale University Research Advisor Kathleen Knafl, PhD, activities within Dr. Knafl's NIH-projects have included development of skill in qualitative and quantitative research techniques including (interviewing skills, questionnaire expert content review, qualitative data analysis for new instrument development, and study submission for Human Subjects Review (3 successfully reviewed applications). All required doctoral core courses have been completed at an Honors or High Pass level of achievement (See Appendix B-Transcript). In addition to core courses, all cognates have been completed. Cognates have focused on advanced research methods (survey, (Dartmouth) qualitative, and quantitative (Yale-School of Public Health), and cancer pharmacology. Furthermore, as planned, the trainee audited two Dartmouth Medical School neurology-focused modules: Introduction to

Neuroscience, and the Neurology section of The Scientific Basis of Medicine (SBM) Course. This coursework has provided solid pathophysiology background for the program of study. At the end of the first year, the trainee passed the Yale required Preliminary (Competency) Exam. All of the above has prepared the trainee to undertake development of the dissertation proposal.

**Task 2. Collect pilot data on peripheral neurological (PN) effects in conjunction with serial neuropsychological and quality of life measures in women enrolled in a longitudinal study of cognitive effects of breast cancer treatment. (Months 1-18)**

The trainee proposed a series of steps to develop the foundational theoretical, instrumental, and clinical skills to perform appropriate assessment of chemotherapy-induced peripheral neuropathy (CIPN). A major finding from the empirical literature review (Please refer to task 3 and see Appendix F) and consultation with neurological experts demonstrated a lack of consensus or gold standard in physical assessment (Cavaletti et al., 2003; Postma & Heimans, 2000; Postma et al., 1999; Postma et al., 1998) and self-reported CIPN and quality of life (Almadrones, McGuire, Walczak, Florio, & Tian, 2004, in press; Blazeby, Sprangers, Cull, Groenvold, & Bottomley, 2001; Calhoun et al., 2003; Cella, Peterman, Hudgens, Webster, & Socinski, 2003). Hence, work items relating to neuropathy assessment have been modified in the following way: the trainee has joined a multidisciplinary project team composed of Dartmouth consultants (Cohen/Fadul/Smith) to develop a pilot project to develop and validate a simplified clinical "reduced" Total Neuropathy Score (TNS)" (Cavaletti et al., 2003; Chaudhry, Chaudhry, Crawford, Simmons-O'Brien, & Griffin, 2003). for use in subsequent CIPN investigations. The project (to be submitted for Hitchcock Foundation funding) intends to establish inter-rater reliability between nurse practitioners (ARNPs) (Bakitas and Smith) and project neurologists using a "reduced / clinical TNS", and then determining concordance between physical exam and sural and peroneal nerve testing. These neurological measures and examination skills will then also be used in "train the trainer" workshops to be presented by the trainee to other DHMC ARNPs as part of a newly funded Oncology Nursing Society grant (See Task 3).

Under the supervision of Dr. Ahles, and (at Yale) Professors Jane Dixon, PhD, and Tish Knobf, PhD, the trainee has conducted an extensive review of literature on CIPN self report QOL instruments. Available instruments are newly developed with only minimal patient-based perspective for item development. Preliminary psychometric properties appear adequate. Based on these finding the trainee has accomplished the following:

- 1) The Functional Assessment for Cancer Therapy-TAXANE (FACT-TAXANE) has been added as the CIPN measure to the battery of assessments of Dr. Ahles Cognitive Effects of Chemotherapy study as planned. Current N=150 breast and lymphoma patients. The FACT-TAXANE has also been incorporated into a newly funded study (Andrew Saykin, PhD-PI and Tim Ahles, PhD-co-PI) entitled "Neuromechanisms of Chemotherapy-Induced Cognitive Disorders". Eleven of one hundred women with breast cancer have already been recruited to this three year companion study. CIPN data will be available for the trainee from both of these studies for future analysis of correlations between PNS and CNS effects of breast cancer treatment; and

2) Evaluation of the patient experience of CIPN and assessment of its impact on QOL, an understudied area and research priority (Oncology Nursing Society, 2003) has become the focus of the trainee's dissertation proposal. Dr. Knobf has agreed to serve as the dissertation chair (along with Ahles, Dixon, and readers McCorkle, and Knafl). This proposal is scheduled for defense in September 2004.

In conjunction with Dr. Ahles the trainee has had an observational experience in Neuropsychological Assessment; no further work is planned on this area given the focus on peripheral assessment.

**Task 3. Identify gaps in knowledge, research hypotheses, and feasible methods to study and develop interventions as a basis for a doctoral dissertation and future program of research (Months 6-24)**

The trainee has been extremely productive in this area. As described an ongoing literature review, established through Dartmouth Medical School Librarian Support, is ongoing, but focused as an independent study in Spring/Summer 2003 on Neurological Effects-See Bibliography Appendix F). Based on the literature the trainee developed two preliminary conceptual models of neurological effects of breast cancer treatment. Appendix C illustrates the trajectory, and Appendix D illustrates the QOL effects specific to CIPN. These models are currently being reviewed and critiqued by consultants (Fadul/Cohen/DeLeo). These models and the review are undergoing further refinement as the basis for the dissertation proposal. An in-depth qualitative exploratory study of the patient's experience of CIPN and its QOL impact is planned. This investigation will contribute to understanding and likely measurement/ instrument refinement and /or development.

The literature synthesis also served as the basis of refinement of Neuropathy Assessment, Referral, and Treatment algorithms. As CO-PI, the trainee assisted PI Smith to submit a clinical research proposal to the Oncology Nursing Foundation to test the integration of these algorithms into clinical practice and evaluate nurse and patient outcomes in summer 2003. Although a good priority score was obtained the proposal was not funded on the first submission. However, reviewer input was incorporated and on resubmission we have just learned that the proposal is now funded (See Appendix E-Study Abstract). The trainee's effort will be contributed as it strengthens and builds upon the current traineeship. No additional salary support is provided through this ONS small grant.

Literature synthesis has also resulted in preparation of a joint lecture, "Neuropathic Pain: From Bench to Bedside" co-taught by Joyce DeLeo, PhD on March 04 at Dartmouth Hitchcock Medical Center.

The trainee will attend three conferences in the coming year that will contribute to knowledge, research networking and dissertation proposal development: 1). July 19-24-University of North Carolina-"Instrument Development"; 2). International Association for the Study of Pain (IASP) Special Interest Group on Pain Conference "Mechanisms and Treatment of Neuropathic Pain" November 4-6, 2004; and 3). the 8<sup>th</sup> National Conference on Cancer Nursing Research, February 3-5, 2005. Abstracts regarding the conceptual models will be submitted to the latter two organizations for consideration for poster/paper presentations.



**Key Research Accomplishments:**

- Completed doctoral coursework
- Passed Preliminary Examination
- Identified Dissertation Committee and Initiated dissertation proposal
- Developed as Co-PI a successfully funded research project on CIPN
- Synthesis and Presentation of CIPN literature for podium, abstract, and dissertation proposal

**Reportable Outcomes:**

All portions of Tasks 1, 2, & 3 due for completion by midterm have been accomplished. In addition, the trainee's contribution as co-investigator to a CIPN clinical research grant has been funded, which will strengthen the program of research and research skills. Two conceptual models developed in preparation for the dissertation proposal will serve as the conceptual model for the study, but will also contribute to the study of neurological effects of breast cancer treatment. Scientific abstracts describing these models are being prepared for submission to scientific meetings.

**Conclusions**

The trainee has made significant progress in acquiring the foundational knowledge and research skills to develop an independent doctoral dissertation in an understudied area of breast cancer research, namely chemotherapy-induced peripheral neuropathy. Via the doctoral dissertation the trainee plans to examine the measurement and patient experience of CIPN and its impact on quality of life and treatment decision-making. This research will contribute to an understanding of this non-life-threatening but dose-limiting effect that can significantly interfere with quality of life. Furthermore, through this mentored, research training program, the trainee has made significant progress in developing a future career in clinical breast cancer research.

**References:**

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## **Appendices**

- A. Statement of Work
- B. Transcript
- C. Conceptual Model of Trajectory of Neurological Effects
- D. Conceptual Model of CIPN Effects on QOL
- E. Abstract of Funded Study
- F. Literature Reviewed for Models and Dissertation Proposal

APPENDIX A.

**Statement of Work**

This statement of work provides an overview of a two year project in which the candidate will spend half of her week on the Yale Campus and half on the Dartmouth Campus.

Task 1. Develop research skills and abilities, including measurement, data analysis, and conceptual model development in breast cancer research through mentorship and doctoral education. (Months 1-18)

1. Weekly meeting with Dr. Ahles for mentored research supervision (Months 1-24)
2. Participate in 15 hrs/wk supervised Research Activities with doctoral faculty (Month 1-18)
3. Complete Year 1-Spring term (Months 1-5) and Year 2 -Fall and Spring (Months 9-17) required doctoral coursework (Yale)
4. Take Research Methods (CECS), Neurology, or Pharmacology Cognates (DMS) (Months 1-5, 9-12, 13-17)
5. Complete Preliminary Exam (at completion of 1<sup>st</sup> year of coursework) Month 6
6. Complete Qualifying Exam (at completion of 2<sup>nd</sup> year of coursework) Month 18
7. Dissertation underway (Month 21-completion)
8. Dissertation advisement (Month 21-completion)

Task 2. Collect pilot data on peripheral neurological (PN) effects in conjunction with serial neuropsychological and quality of life measures in women enrolled in a longitudinal study of cognitive effects of breast cancer treatment. (Months 1-18)

1. Precepted Clinical Neurological Examination Skills (Cohen/Fadul) (Months 1-3)
2. Precepted Neuropsychological Assessment Training (Ahles)
3. Refine and produce standardized neuropathy assessment tool (Cohen/Fadul) (Month 1-5)
4. Develop PN Data Management Procedures (Month 5)
5. Attend weekly meetings of Psychooncology Center for Research and Breast Cancer Tumor Board to identify breast cancer patients on study (Months 6-18)
6. Perform neuropathy assessment on breast cancer patients enrolled in Longitudinal Cognitive Effects (Months 6-18)

Task 3. Identify gaps in knowledge, research hypotheses, and feasible methods to study and develop interventions as a basis for a doctoral dissertation and future program of research (Months 6-24)

1. Perform Review of Literature on Neurological Effects (Months 6-9)
2. Perform Secondary analysis of existing data and summarize preliminary data (months 6-9)
3. Develop draft of a model of neurological effects of breast cancer treatment (Month 10)
4. Call expert panel meeting (Month 10 & 17)
5. Incorporate expert panel comments into model (Month 11-12)
6. Generate list of problems/hypotheses and methods to study, determine feasibility of conducting studies of above, determine funding sources, develop patient educational materials on CNS/PNS effects (Months 12-18)
7. g. Develop dissertation defense based on above to prepare for qualifying exam (Months 12-18)

## APPENDIX B.

# Yale University Student Information System

## Display Transcript



This is NOT an official transcript. A course for which a grade has not been submitted will appear separately under Courses in Progress.

If your course displays with '\*\*\*' in the grade column, you must complete a course evaluation or indicate that you choose not to evaluate the course. Click on the link below the asterisks to go to the course evaluation page.

Transfer Credit   Institution Credit   Courses in Progress

**Transcript Data**

Registration ID:

1025427

\*\*\*This is NOT an Official Transcript\*\*\*

**TRANSFER CREDIT ACCEPTED BY INSTITUTION**   -Top-

Spring 2003:

Dartmouth College

Subject	Course	Title	Grade	Credit Hours
SPRG	2003	Survey Research Methods	CR	3.30

Unofficial Transcript

Spring 2004:

Dartmouth College

Subject	Course	Title	Grade	Credit Hours
SPRG	2004	Health Policy 2	CR	3.30

Unofficial Transcript

**INSTITUTION CREDIT**   -Top-

Fall 2002

College:

Nursing School

Subject	Course Title	Grade	Credit Hours	Grade Mode	Instructor
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NURS	529	Statistics for Clin Nurs Res	H	0.00 Nursing	M. Funk
NURS	901	Methods for Nursing Research	H	3.00 Nursing	J. Dixon
NURS	913	Conceptual Bas for Nsg Science	H	3.00 Nursing	C. Gilliss K. Knafl
NURS	915	Doc Research Prac I	H	1.00 Nursing	R. McCorkle
NURS	943	Conceptual Basis Self/Fam Mgt	H	3.00 Nursing	R. McCorkle G. Melkus K. Knafl

## Unofficial Transcript

Spring 2003

College:

Nursing School

Subject	Course Title	Grade	Credit Hours	Grade Mode	Instructor
NURS	904 Neuro.Effects/Breast CancTrtmt	H	3.00	Nursing	R. McCorkle
NURS	904 Dev.Conc.Rsch.Propsls&Publctns	H	1.00	Nursing	R. McCorkle K. Knafl
NURS	915 Doctoral Research Pract. II	H	1.00	Nursing	R. McCorkle
NURS	917 Adv Stats for Clin Nurs Resrch	H	3.00	Nursing	G. Knafl
NURS	943 Mthlgcl Iss.StudyMgtHlth&Illns	H	3.00	Nursing	M. Grey G. Melkus

## Unofficial Transcript

Fall 2003

College:

Nursing School

Subject	Course Title	Grade	Credit Hours	Grade Mode	Instructor
NURS	805 Cancer Pharmacology	HP	1.50	Nursing	N. Beaulieu
NURS	903 Measurement of Clin Variables	H	3.00	Nursing	J. Dixon
NURS	907 Dissertation Seminar	YR	0.00	Nursing	R. McCorkle
NURS	915 Doctoral Research Pract. II	RE	0.50	Nursing	R. McCorkle

NURS	925	Qualitative Research in Nrsg	H	3.00 Nursing	K. Knafl
NURS	961	Hlth Pol for Pub & Priv Sectrs	HP	3.00 Nursing	S. Cohen

Unofficial Transcript

Spring 2004

College:

Nursing School

Subject	Course Title	Grade	Credit Hours	Grade Mode	Instructor
SOCY	560 Comparative Research Workshop	H	2.00	Nursing	I. Szelenyi A. Schrank

Unofficial Transcript

COURSES IN PROGRESS -Top-

Spring 2004

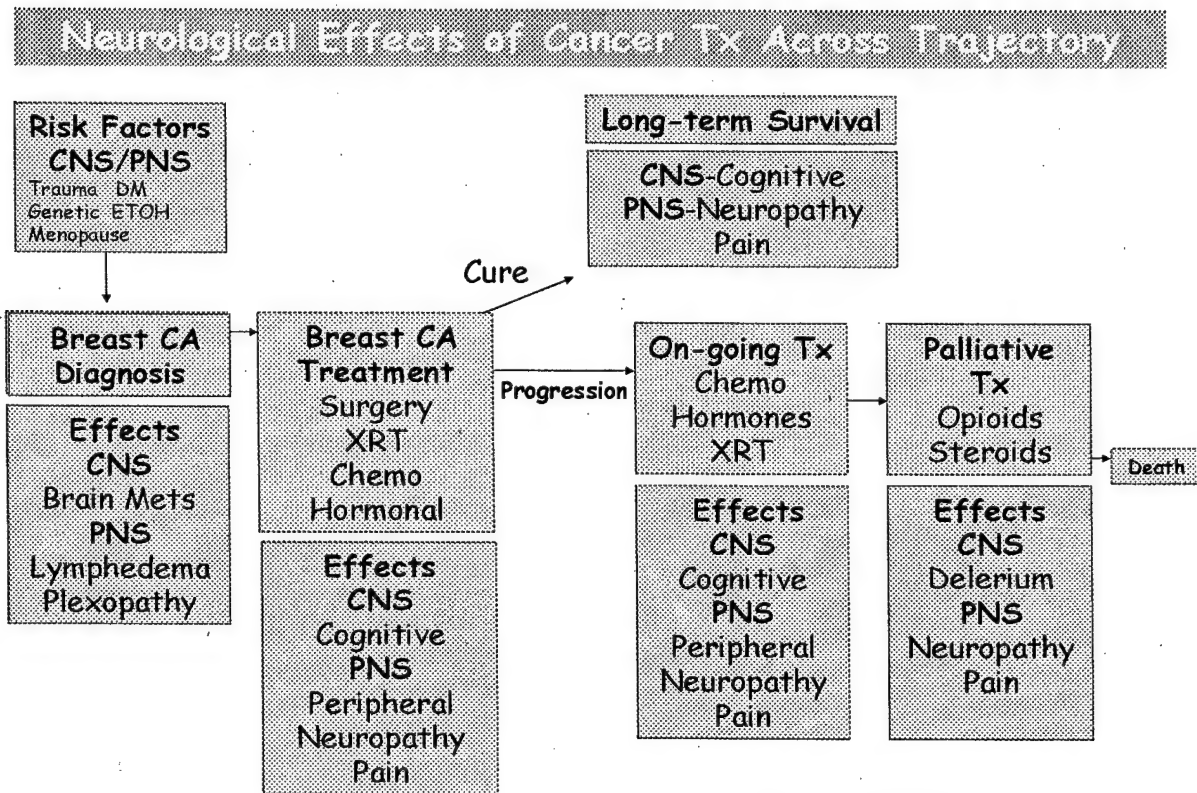
College:

Nursing School

Subject	Course Title	Credit Hours	Grade Mode	Instructor
CDE	534 Approaches to Data Management	3.00	Nursing	M. Desai
NURS	905 CreatingMethod:IssinNursRes	3.00	Nursing	J. Dixon
NURS	907 Dissertation Seminar	3.00	Nursing	M. Grey
NURS	915 Doctoral Research Pract. II	0.50	Nursing	R. McCorkle

RELEASE: 5.5

APPENDIX C.

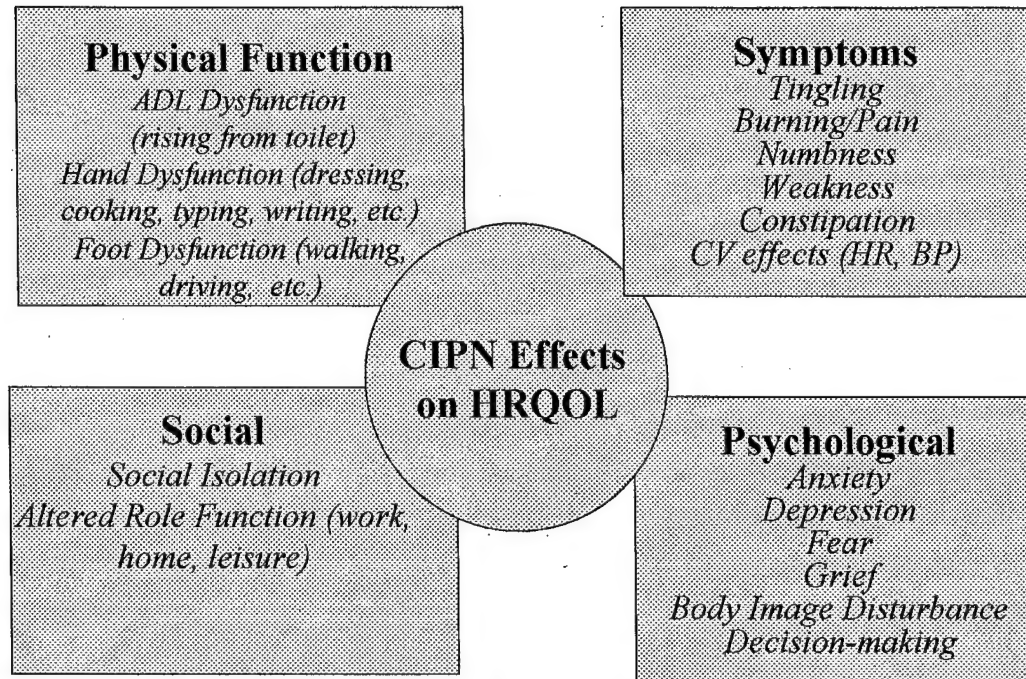


Bakitas. 2003



APPENDIX D.

## Proposed Model of CIPN Effects on QOL \*



\*Based on cancer chemotherapy and DM literature

Bakitas 2003

Smith, Ellen /Neuropathic Pain

## APPENDIX E.

### Testing an Evidenced-Based Treatment and Referral Algorithm in Hematology/Oncology Outpatients with Neuropathic Pain (NP)

**Principal Investigator:** Ellen M. Lavoie Smith, MS, APRN-BC, AOCN **Co-Investigators:** Louise Meyer, MS, ARNP, Marie Bakitas, MS, APRN-BC, AOCN, FAAN, Camilo Fadul, MD; **Dartmouth Hitchcock Medical Center (DHMC)/Norris Cotton Cancer Center (NCCC), Lebanon, NH**

**Consultants:** Marilyn Bookbinder, PhD, RN, Peter Homel, PhD; **Beth Israel Medical Center, New York, NY**

#### Abstract

#### Purpose/Specific Aims:

The specific aims of this study are:

1. To implement an evidence-based screening, assessment, treatment and referral guideline for hematology/oncology outpatients with neuropathic pain (NP) receiving care at a comprehensive cancer center and 6 affiliated rural outreach clinics; and

2. To pilot-test the efficacy of an NP Algorithm on patient outcomes (pain experience, activities of daily living), and patient perceptions of the assessment/treatment process.

**Rationale and Significance:** Neuropathic pain is defined as pain that arises from injury, disease, or dysfunction of the central or peripheral nervous system. NP is described as burning, numbness, stabbing, pricking, tingling, sharpness, shooting, or electric-shock-like. NP is estimated to affect more than 2 million Americans, and suffering can be severe and persist for months to years. Historically NP has been inadequately assessed by healthcare professionals and underreported by patients. Data suggests that healthcare professionals lack knowledge regarding effective NP assessment and management strategies. Investigations of NP analgesic efficacy have provided little evidence to guide practitioners when selecting, titrating, and rotating analgesic combinations with different mechanisms of action. Therefore, evidence-based guidelines defining drug choice, combinations, dosage, sequence, and treatment duration have not been systematically implemented or tested. Suboptimal assessment practices and scant knowledge of "best practice" algorithms contribute to a high prevalence of uncontrolled NP and negative effects on patients' quality of life.

**Guideline to Be Implemented:** The NP evidence-based algorithm to be pilot-tested builds upon this Investigative Team's earlier ONF-funded project, "QUEST for PAIN Relief (2000-2001). QUEST developed an infrastructure to raise the standard of oncology patient care by fostering evidenced-based practice, utilization of research findings, and the generation of future research. Ellen Smith (PI), one of five advanced practice nurses mentored by the researcher-clinician team (Bookbinder and Whedon) served as a formal linkage agent, using a continuous quality improvement approach, to develop the NP guideline piloted in this project.

**Practice Change:** The recommended practice change involves implementation of NP assessment and treatment guidelines using a proven quality improvement model and multi-level educational strategies to change practice patterns and improve outcomes in identified patients with NP. Strategies involve traditional educational approaches in a cancer center and six outreach sites via in-services, audit-feedback, and clinical system changes through integrating an evidence-based algorithm into practice standards and ongoing communication via an electronic "community of practice" site throughout the grant period. Other innovative educational approaches include case-based nurse education and practice-linked reminders such as laminated pocket cards and posters reinforcing assessment, treatment, and referral guidelines. Outpatients with NP ratings greater than 4 on a 0-10 pain scale will be identified by nursing assistants and staff nurses for a follow-up neurological exam by the nurse practitioner and initiation of the treatment algorithm when appropriate. The algorithm study team and site-specific QI teams will meet at least bimonthly to evaluate and communicate progress throughout all study phases.

**Evaluation Plan:** Evaluation includes: ARNP clinical competency in NP assessment and management, chart audit for algorithm adherence and efficacy, and patient outcomes using standardized assessment tools.

APPENDIX F.

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